Interagency Coordinating Committee on the Validation of Alternative Methods

Implementation Plan for P. L. 106-545

1.0 PURPOSE

The purpose of this document is to describe the general plan for the review evaluation of new and revised toxicological methods pursuant to P. L. 106-545.

2.0 BACKGROUND

2.1

This proposed implementation plan is based in part on: (1) implementation procedures outlined in the 1997 Report of the ad hoc ICCVAM: *Validation and Regulatory Acceptance of Toxicological Test Methods* (NIH Publication 97-3981); (2) procedures developed and implemented by the ICCVAM during its operation from May 1997 to the present; and (3) the publication *Evaluation of the Validation Status of Toxicological Methods: General Guidelines for Submissions to ICCVAM*, (NIH Publication No. 99-4496, October 1999).

2.2 NICEATM

In April 1998, the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) was established to provide operational support for the ICCVAM and to carry out related activities. From 1998 to 2000, the ICCVAM and the NICEATM:

- published guidelines for the submission of test methods to ICCVAM;
- organized the interagency scientific evaluation of five toxicity testing methods submitted to ICCVAM;
- forwarded test method recommendations for acceptance consideration to Federal agencies;
- convened the first test method implementation workshop to facilitate use of a new improved test method; and
- coordinated interagency responses on validation issues and proposed international test guidelines

2.3 ICCVAM Authorization Act

The ICCVAM Authorization Act of 2000, Public Law 106-545, was signed by the President on December 19, 2000. This law establishes ICCVAM as a permanent interagency coordinating committee. It mandates the 15 agencies that are represented on the ICCVAM, and specifies the purposes and duties of ICCVAM as follows:

2.4 Purposes of ICCVAM[1] (P. L. 106-545, Section 3(b))

(1) Increase the efficiency and effectiveness of Federal agency test method review;
(2) Eliminate unnecessary duplicative efforts and share experiences between Federal regulatory agencies;
(3) Optimize utilization of scientific expertise outside the Federal Government;

(4) Ensure that new and revised test methods are validated to meet the needs of Federal agencies; and
(5) Reduce, refine, and replace the use of animals in testing, where feasible.

2.5 Duties of the ICCVAM[1] (P. L. 106-545, Section 3(e))

(1) Review and evaluate new or revised or alternative test methods, including batteries of tests and test screens, that may be acceptable for specific regulatory uses, including the coordination of technical reviews of proposed new or revised or alternative test methods of interagency interest.
(2) Facilitate appropriate interagency and international harmonization of acute or chronic toxicological test protocols that encourage the reduction, refinement, or replacement of animal test methods.
(3) Facilitate and provide guidance on the development of validation criteria, validation studies and processes for new or revised or alternative test methods and help facilitate the acceptance of such scientifically valid test methods and awareness of accepted test methods by Federal agencies and other stakeholders.
(4) Submit ICCVAM test recommendations for the test method reviewed by the ICCVAM, through expeditious transmittal by the Secretary of Health and Human Services (or the designee of the Secretary), to each appropriate Federal agency, along with the identification of specific agency guidelines, recommendations, or regulations for a test method, including batteries of tests and test screens, for chemicals or class of chemicals within a regulatory framework that may be appropriate for scientific improvement, while seeking to reduce, refine, or replace animal test methods. [This activity is fully delegated by ICCVAM to the Director of NIEHS.]
(5) Consider for review and evaluation, petitions received from the public that-
(A) identify a specific regulation, recommendation, or guideline regarding a regulatory mandate; and
(B) recommend new or revised or alternative test methods and provide valid scientific evidence of the potential of the test method.
(6) Make available to the public final ICCVAM test recommendations to appropriate Federal agencies and the responses from the agencies regarding such recommendations. [This activity is fully delegated by ICCVAM to the Director of NIEHS.]
(7) Prepare reports to be made available to the public on its progress under this Act. The first report shall be completed not later than 12 months after the date of the enactment of this Act, and subsequent reports shall be completed biennially thereafter. . [Authority for this activity is fully delegated by ICCVAM to the Director of NIEHS.]

---

[1]*Italicized text is from P. L. 106-545 as noted.*

3.0 PLAN

The following describes the general plan for the review and evaluation of toxicological methods by ICCVAM pursuant to P. L. 106-545. Other operating procedures will be established by the ICCVAM as necessary, and this document will be updated periodically, as appropriate.

3.l Designation of Agency Representatives[1] (P. L. 106-545, Section 3(c))

The Committee consists of agency heads or their designees from each of the following agencies:

Agency for Toxic Substances and Disease Registry
Consumer Product Safety Commission
Department of Agriculture
Department of Defense
Department of Energy
Department of Interior
Department of Transportation
Environmental Protection Agency
Food and Drug Administration
National Cancer Institute
National Institute of Environmental Health Sciences
National Institutes of Health, Office of the Director
National Institute of Occupational Safety and Health
National Library of Medicine
Occupational Safety and Health Administration

The Agency Head or his/her designee is the principal agency representative on ICCVAM. Each agency shall designate one or more alternate representatives. Agencies may designate additional liaison representatives as deemed appropriate.

3.2 Agency Responsibilities

- Obtain and disseminate information on issues discussed by the ICCVAM.
- Identification of technical experts from their agency/program to serve on specific test method workgroups.
- Agency principal representatives will serve as nonvoting ex officio members of the Advisory Committee on Alternative Toxicological Methods (Section 3(d)(2)(B), P.L. 106-545).

3.3 Call for Meetings

The Chair will call for regular and special meetings of the ICCVAM. Regular meetings will be scheduled in advance to ensure attendance by the maximum number of representatives as possible. Special meetings will be called by the Chair to consider only urgent matters that cannot be deferred until a regularly scheduled meeting. When deemed necessary for expeditious actions, the Chair may convene meetings via teleconference or videoconference.

[1] *Italicized text is from P. L. 106-545 as noted.*

3.4 Quorum
A quorum will be considered present when a simple majority of the principal agency representatives or their alternates is in attendance.

3.5 Election of the Chair
The ICCVAM will elect a Chair and Vice-Chair biennially. The Chair and Vice-Chair may serve multiple terms.

3.6 Absence of the Chair
In the absence of the Chair, the Vice-Chair will chair meetings of the Committee. In addition, if the Chair is unavailable, the Vice-Chair may call special meetings of the Committee to consider particularly urgent matters.

3.7 Establishment of Working Groups
- The ICCVAM will establish working groups as necessary on either an ad hoc or standing basis. These working groups will report directly to ICCVAM.
- The Director of NICEATM will coordinate NICEATM staff support for each subcommittee and working group as resources permit.

3.8 Conduct of Meetings
The ICCVAM will approve procedures for conducting meetings.

3.9 Meeting Procedures
- Meeting agendas. The Chair and Director of NICEATM will develop meeting agendas and seek input for the agenda from ICCVAM representatives.
- Program support staff. The Director of NICEATM will provide NICEATM staff necessary to support deliberations of the Committee, to the extent that resources permit.
- Minutes. The Director of NICEATM or his/her designee will prepare draft minutes of each meeting, which will be distributed and finalized following review and approval by the Committee.
- Meetings of the Committee will be closed to the public and attendance limited to designated ICCVAM representatives, NICEATM staff, and invited guests. Individuals may be invited to attend all or a specified portion of a meeting on a case-specific basis in accordance with Federal meeting regulations.

3.10 Distribution of ICCVAM Documents:
3.10.1 On behalf of the ICCVAM, the Director of NIEHS will, in accordance with P.L. 106-545, Section 3(e):
- Submit ICCVAM test recommendations through expeditious transmittal by the Secretary, DHHS, (or the designee of the Secretary) to each appropriate Federal agency, including the identification of existing testing requirements for which the test recommendations may be applicable as an improvement, or that will further refine, reduce, or replace animal use.

- Make available to the public final ICCVAM test recommendations to appropriate Federal agencies and the responses from the Agencies regarding such recommendations.
- Prepare reports to be made available to the public on its progress under this Act. The first report shall be completed no later than 12 months after the date of the enactment of this Act [December 19, 2001], and subsequent reports shall be completed biennially thereafter.

3.10.2 The Director of NICEATM will also prepare and distribute such things as the following documents to the ICCVAM:

- Meeting agenda.
- Meeting minutes.
- Meeting documents.
- Test method submissions, petitions, and nominations, including NICEATM executive summaries of their completeness and applicability (see Section 3.12).
- Peer review panel and workshop reports.

3.10.3 The Director of NICEATM will prepare appropriate summaries and notices of the following for publication in the *Federal Register*, and otherwise make these available to the public including such things as:

- Scheduled peer review meetings and workshops.
- Scheduled meetings of the Scientific Advisory Committee.
- NICEATM peer review meeting and workshop reports.
- ICCVAM test method recommendations.
- Annual/biennial reports.

3.11 Consideration of Test Methods for ICCVAM Review and Evaluation

- Validated test methods proposed to ICCVAM for review and evaluation (including petitions received from the public) will be considered as test method submissions. Test methods proposed for validation studies will be considered as test method nominations. The Director of NICEATM will solicit and track the status of test method submissions and nominations and provide updates to the ICCVAM.
- The Director of NICEATM will arrange for preliminary evaluation of test method submissions and nominations by the NICEATM, as resources permit. The preliminary evaluation will address the following:
    - The completeness of the submission with regard to ICCVAM test method submission guidelines.
    - The extent to which the proposed method is applicable to regulatory testing needs.
    - The potential for the method to provide improved prediction of an adverse health or environmental effect compared to current methods.
    - The extent to which the test method provides other advantages, such as reduced cost and time to perform, compared to current methods.

  - The extent to which the test method is applicable to multiple agencies/programs.
  - The potential for the method to refine, reduce, and/or replace animal use, compared to current methods.
- The Director of NICEATM will provide the results of NICEATM preliminary evaluations and recommendations regarding priority for further evaluation to the ICCVAM.
- ICCVAM will recommend whether the method is of sufficient interagency interest and applicability to warrant further evaluation or validation studies, and will recommend a priority for such evaluation or validation studies.
- The Director of NICEATM will provide the Advisory Committee on Alternative Toxicological Methods (ACATM) with an updated status report on test method submissions and nominations, including the results of NICEATM and ICCVAM preliminary evaluations and recommendations. The ACATM will be asked to provide advice on test method evaluation and validation study priorities. [Note: ACATM meetings are open to the public in accordance with Federal Advisory Committee Act provisions which include provision of an agenda and background material at least 30 days prior to a meeting.]
- All test method submissions and nominations along with ICCVAM, NICEATM, and ACATM priority recommendations are forwarded by the Director of NICEATM to the Associate Director of the NTP. The Associate Director of the NTP uses these recommendations to determine what resources to commit for the proposed evaluations or validation studies.
- When resources are approved to support the necessary evaluation (e.g., independent peer review) or validation study, an ICCVAM test method working group composed of knowledgeable scientists from participating agencies will be established to work with the NICEATM to organize the appropriate evaluation or validation study. With the advice of ICCVAM, NICEATM will establish peer review groups and organize workshops as necessary to address the scientific validation of alternative methods. These peer review groups and workshop panels will report directly to the Director of NICEATM who will transmit the report through the appropriate Working Group to ICCVAM. Final decisions on membership of independent peer review panels are the responsibility of the Associate Director of the NTP with recommendations from ICCVAM and NICEATM.
- Test methods will be evaluated by independent peer review panels to determine the extent to which established ICCVAM validation and acceptance criteria have been addressed, to address case specific questions, and to determine their usefulness and limitations for a specified purpose. Reports will be prepared and published that include the peer review panel assessments and summarize the data and information used for the evaluation of test methods. ICCVAM will review these test method evaluations and, in accordance with P.L. 106-545, develop ICCVAM test recommendations for submission to appropriate Federal Agencies. ICCVAM test recommendations will be forwarded to ICCVAM agencies by the Secretary, DHHS, or designee, for acceptance consideration and decision in accordance with Section 4, P.L. 106-545.

- Per Section 4 of P.L 106-545, Federal agencies will, within 180 days after receipt of an ICCVAM test recommendation: (1) review the recommendation and notify the Director of the NIEHS of its findings; and (2) identify and forward to the NICEATM any relevant test method for which the ICCVAM test recommendation may be added or substituted. NICEATM will collect these responses and distribute them to all ICCVAM member agencies, ACATM, and any other interested parties.
- Decisions on test method acceptance are the responsibility of individual agencies according to their statutory mandates. Per P. L. 106-545[1], Section 4 (e): *Each Federal agency carrying out a program described in subsection 4(a), or its specific regulatory unit or units, shall adopt the ICCVAM test recommendations unless such Federal agency determines that:*
  - (*1) the ICCVAM test recommendation is not adequate in terms of biological relevance for the regulatory goal authorized by that agency, or mandated by Congress;*
  - *(2) the ICCVAM test recommendation does not generate data, in an amount and of a scientific value that is at least equivalent to the data generated prior to such recommendation, for the appropriate hazard identification, dose-response assessment, or risk assessment purposes as the current test method recommended or required by that agency;*
  - *(3) the agency does not employ, recommend, or require testing for that class of chemical or for the recommended test endpoint; or*
  - *(4) the ICCVAM test recommendation is unacceptable for satisfactorily fulfilling the test needs for that particular agency and its respective congressional mandate.*

Adopted by ICCVAM:
August 27, 2001

[1] *Italicized text is from P. L. 106-545 as noted.*